which effects reduction of the particular condition, or retards its expansion. When **co-administering** the compounds of the invention to block retinoid-induced toxicity or side effects, the antagonist and/or inverse agonist compounds of the. . .

ACCESSION NUMBER: 2001:22395 USPATFULL

TITLE: Substituted diaryl or diheteroaryl methanes, ethers and amines having retinoid agonist, antagonist or inverse agonist type biological

INVENTOR(S): Song, Tae K., 3768 N. Country Club Dr., Long Beach, CA, United States 90807
Teng, Min, 2 Dove St., Aliso Viejo, CA, United States 92656
Chandraratna, Roshantha A., 25841 Empresa, Mission Viejo, CA, United States 92691

	NUMBER	DATE
PATENT INFORMATION:	US 6187950	20010213
APPLICATION INFO.:	US 1999-267992	19990312 (9)

RELATED APPLN. INFO.: Division of Ser. No. US 1997-840040, filed on 24 Apr 1997, now patented, Pat. No. US 5919970

DOCUMENT TYPE: Utility

PRIMARY EXAMINER: Raymond, Richard L.

LEGAL REPRESENTATIVE: Szekeres, Gabor L.; Baran, Robert J.; Voet, mARTIN A.

NUMBER OF CLAIMS: 7

EXEMPLARY CLAIM: 1

LINE COUNT: 2502

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

CLM What is claimed is:

1. A compound of the formula ##STR13## where R.sub.4 is H or F; R.sub.2 is fluoro-substituted alkyl of 1 to 6 carbons, NO.sub.2, NH.sub.2, COOC.sub.1-6 alkyl, N.sub.3 or I; R.sub.4 * is H, F, NO.sub.2 or NH.sub.2 ; Z is --C.tbd.C--, --CH.dbd.CH

L17 ANSWER 2 OF 12 CAPLUS COPYRIGHT 2001 ACS
AN 1996:745366 CAPLUS
DN 126:14397
TI **Sequential** antibiotic **therapy** for **acne** promotes the carriage of resistant staphylococci on the skin of contacts
AU Miller, Yvonne W.; Eady, E. Anne; Lacey, Richard W.; Cove, Jonathan H.; Joanes, Derrick N.; Cunliffe, William J.
CS Department Microbiology, University Leeds, Leeds, LS2 9JT, UK
SO J. Antimicrob. Chemother. (1996), 38(5), 829-837
CODEN: JACHDX; ISSN: 0305-7453
PB Saunders
DT Journal
LA English
CC 1-5 (Pharmacology)
AB The selection of a predominantly resistant staphylococcal skin flora in **acne** patients during antibiotic **treatment** has been extensively documented. This study sought to det. whether antibiotic **therapy** for **acne** had any effect on skin carriage of resistant coagulase-neg. staphylococci (CNS) by close contacts of treated patients. Bacterial samples were obtained using a scrub wash technique from facial skin of 41 contacts (parents, siblings or partners) of patients who had been treated with at least three different antibiotics over a min. period of 2 yr. Samples were also obtained from 41 control subjects who had no known contact with any antibiotic treated **acne** patient. None of the contacts or controls had received any antibiotic **therapy** in the preceding two years. The no., percentage and prevalence of CNS resistant to each of seven antibiotics was estd. by plating serial ten-fold dilns. of wash fluid directly onto antibiotic-contg. and antibiotic-free medium. Significantly more contacts than controls carried strains resistant to erythromycin, clindamycin, fusidic acid, trimethoprim and chloramphenicol as well as more multiply resistant strains ($P < 0.05$, .chi.2). The no. and percentage of staphylococci resistant to tetracycline, erythromycin, clindamycin, fusidic acid and chloramphenicol were also significantly raised ($P < 0.05$, Mann-Whitney U-test) in contacts. Only aminoglycoside resistance was not increased by any of the above criteria. These observations provide evidence that **sequential** antibiotic **therapy** for **acne** exerts selective pressure for increased skin carriage of resistant CNS not only in patients but also in their close contacts.
ST antibiotic staphylococci drug resistance
IT Antibiotics
Drug resistance
Staphylococcus
(**sequential** antibiotic **therapy** for **acne** promotes the carriage of resistant staphylococci on the skin of contacts in humans)
IT 60-54-8, Tetracycline 79-57-2, Oxytetracycline 114-07-8, Erythromycin 564-25-0, Doxycycline 738-70-5, Trimethoprim 10118-90-8, Minocycline
RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**sequential** antibiotic **therapy** for **acne** promotes the carriage of resistant staphylococci on the skin of contacts in humans)

=>

L20 ANSWER 20 OF 23 CAPLUS COPYRIGHT 2001 ACS
TI Treatment of inflammatory dermatoses with corticosteroids and **retinoids**
AB Inflammatory dermatoses (e.g. **acne**, lichen planus, mycosis fungoides, acute drug reactions, but not psoriasis) are controlled and cleared by topical application to the affected area of a synergistic combination of a corticosteroid and a **retinoid**. Thus, chronic atopic dermatitis was treated twice daily with a cream contg. 0.025 or 0.05% tretinoin and 2.0% hydrocortisone; the. . .
ST dermatitis treatment corticosteroid **retinoid**
IT Allergy inhibitors
(corticosteroid-**retinoid** combinations, contact dermatitis and dermatitis from drug hypersensitivity treatment with)
IT Inflammation inhibitors
(corticosteroid-**retinoid** combinations, dermatitis treatment with)
IT Pharmaceuticals
(hypersensitivity to, dermatitis from, **treatment** of, with corticosteroid-**retinoid combination**)
IT **Retinoids**
RL: BIOL (Biological study)
(mixts. with corticosteroids, dermatitis treatment with)
IT Corticosteroids, biological studies
RL: BIOL (Biological study)
(mixts. with **retinoids**, dermatitis treatment with)
IT **Acne**
Dermatitis
(**treatment** of, with corticosteroid-**retinoid combination**)
IT Alopecia
(areata, **treatment** of, with corticosteroid-**retinoid combination**)
IT Lupus erythematosus
(discoid, **treatment** of, with corticosteroid-**retinoid combination**)
IT Keratosis
(follicularis, **treatment** of, with corticosteroid-**retinoid combination**)
IT Skin, disease
(lichen planus, **treatment** of, with corticosteroid-**retinoid combination**)
IT Skin, neoplasm
(mycosis fungoides, **treatment** of, with corticosteroid-**retinoid combination**)
IT Skin, disease
(pseudofolliculitis barbae, **treatment** of, with corticosteroid-**retinoid combination**)
IT 68-26-8D, Retinol, mixts. with corticosteroids 76-25-5D, Triamcinolone acetonide, mixts. with **retinoids** 79-81-2D, Retinyl palmitate, mixts. with corticosteroids 116-31-4D, Retinal, mixts. with corticosteroids 302-79-4D, all-trans-Retinoic acid, mixts. with corticosteroids 401-10-5D, Retinoyl .beta.-glucuronide, mixts. with corticosteroids 2152-44-5D, Betamethasone valerate, mixts. with **retinoids** 4759-48-2D, 13-cis-Retinoic acid, mixts. with corticosteroids 5300-03-8D, 9-cis-Retinoic acid, mixts. with corticosteroids 7069-42-3D, Retinyl propionate, mixts. with corticosteroids 25122-46-7D, Clobetasol propionate, mixts. with **retinoids** 51077-50-0D, mixts. with corticosteroids 54350-48-0D, mixts. with corticosteroids 55079-83-9D, mixts. with

corticosteroids 56281-36-8D, mixts. with corticosteroids 68070-35-9D, 11-cis-Retinoic acid, mixts. with corticosteroids 69251-08-7D, mixts. with corticosteroids 71441-28-6D, mixts. with corticosteroids 75078-91-0D, mixts. with corticosteroids 75664-66-3D, mixts. with corticosteroids 78548-88-6D, mixts. with corticosteroids 79073-30-6D, mixts. with corticosteroids 79073-31-7D, mixts. with corticosteroids 83860-24-6D, mixts. with corticosteroids 86471-13-8D, mixts. with corticosteroids 86471-16-1D, mixts. with corticosteroids 87719-32-2D, mixts. with corticosteroids 91587-01-8D, mixts. with corticosteroids 94497-51-5D, mixts. with corticosteroids 102121-60-8D, mixts. with corticosteroids 103810-85-1D, 4-Acetamidophenyl retinoate, mixts. with corticosteroids 104458-65-3D, mixts. with corticosteroids 104561-36-6D, mixts. with corticosteroids 104561-41-3D, mixts. with corticosteroids 106685-40-9D, mixts. with corticosteroids 131331-37-8D, mixts. with corticosteroids 133207-56-4D, mixts. with corticosteroids 150406-02-3D, mixts. with corticosteroids
RL: BIOL (Biological study)
(dermatitis treatment with)

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9315740	A1	19930819	WO 1993-US1043	19930129
	W: AU, CA, CZ, FI, JP, KR, NO, NZ				
	RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
	AU 9335854	A1	19930903	AU 1993-35854	19930129
	AU 667519	B2	19960328		
	EP 625045	A1	19941123	EP 1993-904929	19930129
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
	JP 07505617	T2	19950622	JP 1993-514192	19930129
	JP 2927961	B2	19990728		
	ZA 9300811	A	19930910	ZA 1993-811	19930205
	US 5998395	A	19991207	US 1993-119510	19930910
	FI 9403625	A	19940804	FI 1994-3625	19940804
	NO 9402913	A	19941005	NO 1994-2913	19940805

L20 ANSWER 16 OF 23 CAPLUS COPYRIGHT 2001 ACS
TI **Combination** method for **acne treatment**
AB Described is a **combination** method using selective inhibitors of 5.alpha.-reductase 1 and/or 2 including 7.beta.-substituted 3-aza-5.alpha.-cholestan-3-ones and related 4-aza-5.alpha.-androstan-3-one compds. which are useful in the **treatment** of **acne** vulgaris in **combination** with a **retinoid**, e.g., tretinoin or isotretinoin, and at least one agent selected from an antibacterial, keratolytic, and/or an anti-inflammatory (no data). The. . .
ST **acne** treatment azacholestanone azaandrostanone prepn; reductase inhibitor azacholestanone azaandrostanone prepn
IT **Acne**
(prepn. of azacholestanones and azaandrostanones as reductase inhibitors in **acne** treatment)

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 9612487	A1	19960502	WO 1995-US13305	19951017
W: AL, AM, AU, BB, BG, BR, BY, CA, CN, CZ, EE, FI, GE, HU, IS, JP, KG, KR, KZ, LK, LR, LT, LV, MD, MG, MK, MN, MX, NO, NZ, PL, RO, RU, SG, SI, SK, TJ, TM, TT, UA, US, UZ				
RW: KE, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
CA 2199979	AA	19960502	CA 1995-2199979	19951017
AU 9538336	A1	19960515	AU 1995-38336	19951017
AU 694576	B2	19980723		
EP 786999	A1	19970806	EP 1995-936349	19951017
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
JP 10508586	T2	19980815	JP 1996-514031	19951017

L20 ANSWER 17 OF 23 CAPLUS COPYRIGHT 2001 ACS
AB Minocycline, a semisynthetic deriv. of **tetracycline**, has become a commonly prescribed medication for the **treatment** of persistent **acne**. It has been assocd. with a variety of adverse reactions, including one published case of serum sickness. We describe two. . . sickness reactions due to minocycline, characterized by erythematous rash, arthropathy, and in one case, angioedema. Both patients recovered fully after **treatment** with an antihistamine in **combination** with a brief course of corticosteroids. Although these represent only the second and third cases in the literature of minocycline-induced. . .

L20 ANSWER 13 OF 23 CAPLUS COPYRIGHT 2001 ACS
TI Skin care compositions containing naringenin and/or quercetin and a **retinoid**
AB Quercetin and/or naringenin (I) in **combination** with either retinol (II) or retinyl ester resulted in a synergistic inhibition of keratinocyte differentiation. The effects of the retinol or retinyl esters in **combination** with naringenin and/or quercetin were analogous to **treatment** with retinoic acid. Commination of 2.5x10-9 M II and 10-9 M I inhibited keratinocyte differentiation by 53%. A cosmetic emulsion. . .
ST skin keratinocyte differentiation naringenin quercetin **retinoid**; cosmetic emulsion naringenin retinol
IT Skin aging
(disorder, photoaging; skin care compns. contg. naringenin and/or quercetin and **retinoid**)
IT Skin diseases
(dry skin; skin care compns. contg. naringenin and/or quercetin and **retinoid**)
IT Skin diseases
(photoaging; skin care compns. contg. naringenin and/or quercetin and **retinoid**)
IT **Acne**
Atopic dermatitis
Cell differentiation
Cosmetic emulsions
Keratinocyte
Lotions (cosmetics)
Sebum
Sunscreens
(skin care compns. contg. naringenin and/or quercetin and **retinoid**)
IT **Retinoids**
RL: BAC (Biological activity or effector, except adverse); BUU (Biological use, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(skin care compns. contg. naringenin and/or quercetin and **retinoid**)
IT Flavonoids
RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(skin care compns. contg. naringenin and/or quercetin and **retinoid**)
IT Cosmetics
(wrinkle-preventing; skin care compns. contg. naringenin and/or quercetin and **retinoid**)
IT 68-26-8, Retinol 79-81-2, Retinyl palmitate 117-39-5, Quercetin 480-41-1, Naringenin 7069-42-3, Retinyl propionate
RL: BAC (Biological activity or effector, except adverse); BUU (Biological use, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(skin care compns. contg. naringenin and/or quercetin and **retinoid**)
IT 127-47-9, Retinyl acetate 302-79-4, Retinoic acid
RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(skin care compns. contg. naringenin and/or quercetin and **retinoid**)

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 5665367	A	19970909	US 1996-722540	19960927

L20 ANSWER 8 OF 23 CAPLUS COPYRIGHT 2001 ACS
TI Serine proteinase and topical **retinoid** compns. for treatment of **acne** and inhibition of skin aging
AB This invention is related to methods for treating **Acne** Vulgaris and/or for producing anti-aging effects on the skin of a mammal, and compns. effective for the same. More specifically,. . . invention is directed to the use of serine proteases, as the sole active agent in a compn. effective for the **treatment** of **Acne** Vulgaris and/or for producing anti-aging effects on the skin of a mammal, or in **combination** with a **retinoid** compd. in a compn. effective for the same.
ST serine proteinase topical **retinoid** formulation **acne**; antiaging skin serine proteinase **retinoid** formulation
IT Mouse
(Rhino mouse; serine proteinase and topical **retinoid** compns. for treatment of **acne** and inhibition of skin aging)
IT Cosmetics
(adjuvants; serine proteinase and topical **retinoid** compns. for treatment of **acne** and inhibition of skin aging)
IT Apoptosis
(inhibition of; serine proteinase and topical **retinoid** compns. for treatment of **acne** and inhibition of skin aging)
IT Liposomes (drug delivery systems)
(nonionic; serine proteinase and topical **retinoid** compns. for treatment of **acne** and inhibition of skin aging)
IT Aging (animal)
Antioxidants (pharmaceutical)
Buffers
Coloring materials
Foaming agents
Humectants
Moisturizers (cosmetics)
Perfumes
Preservatives
Skin conditioners
Sunscreens
Surfactants
Thickening agents
Topical drug delivery systems
(serine proteinase and topical **retinoid** compns. for treatment of **acne** and inhibition of skin aging)
IT **Retinoids**
RL: BAC (Biological activity or effector, except adverse); BUU (Biological use, unclassified); PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(serine proteinase and topical **retinoid** compns. for treatment of **acne** and inhibition of skin aging)
IT Hair follicle
(trypsin delivery into; serine proteinase and topical **retinoid** compns. for treatment of **acne** and inhibition of skin aging)
IT **Acne**
(vulgaris; serine proteinase and topical **retinoid** compns. for treatment of **acne** and inhibition of skin aging)
IT 68-26-8, Vitamin a alcohol 79-81-2, Retinyl palmitate 116-31-4, Retinal 127-47-9, Retinyl acetate 302-79-4, Retinoic acid 9001-92-7, Proteinase 9002-07-7, Trypsin 9014-01-1, Subtilisin 9046-67-7, Carboxypeptidase Y 37259-58-8, Serine proteinase 97501-93-4, Tryptase

RL: BAC (Biological activity or effector, except adverse); BUU (Biological use, unclassified); PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(serine proteinase and topical **retinoid** compns. for treatment of **acne** and inhibition of skin aging)

IT 57-88-5, Cholesterol, biological studies 1323-83-7, Glycerol distearate 9005-00-9, Polyoxyethylene stearyl ether 27638-00-2, Glycerol dilaurate
RL: PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(serine proteinase and topical **retinoid** compns. for treatment of **acne** and inhibition of skin aging)

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9848775	A1	19981105	WO 1998-US2618	19980206

W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE,

L31 ANSWER 7 OF 18 USPATFULL

SUMM . . . are effective in treating arthritis. See, for example, Greenwald et al., "Tetracyclines Suppress Metalloproteinase Activity in Adjuvant Arthritis and, in **Combination** with Flurbiprofen, Ameliorate Bone Damage," Journal of Rheumatology 19:927-938(1992); Greenwald et al., "**Treatment** of Destructive Arthritic Disorders with **MMP Inhibitors**: Potential Role of Tetracyclines in, Inhibition of Matrix Metalloproteinases:Therapeutic Potential," Annals of the New York Academy of Sciences 732: 181-198. . . et al., "Potential of Tetracycline to Modify Cartilage Breakdown in Osteoarthritis," Current Opinion in Rheumatology 8: 238-247(1996); O'Dell et al., "**Treatment** of Early Rheumatoid Arthritis with Minocycline or Placebo," Arthritis Rheum 40:842-848(1997).

SUMM The use of tetracyclines in **combination** with non-steroidal anti-inflammatory agents has been studied in the **treatment** of inflammatory skin disorders caused by **acne** vulgaris. Wong et al., Journal of American Academy of Dermatology 1: 1076-1081 (1984), studied the **combination** of tetracycline and ibuprofen and found that tetracycline was an effective agent against **acne** vulgaris while ibuprofen was useful in reducing the resulting inflammation by inhibition of cycloxygenase. Funt et al., Journal of the. . .